



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

David Lane *et al.*

Application Serial No. 09/214,371

Filed: March 26, 1999

For: ***Inhibitors of the Interaction  
Between p53 and mdm2***

) Examiner: Zara, Jane J.  
)  
) Art Unit: 1635  
)  
) Confirmation No.: 8832  
)  
) **Customer No. 25213**  
)  
)

**INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97**

Express Mail No.: EL 993 633 767 US  
Mailing Date: March 2, 2005

Mail Stop: RCE  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Listed below or on an attached Substitute Form PTO-1449 is information known to applicants. A copy is provided of each foreign patent, each cited pending unpublished U.S. application, and all additional publications other than U.S. patents and U.S. patent application publications. 37 C.F.R. §§1.97-1.98.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. If form Substitute PTO-1449 is enclosed, the Examiner is requested to initial and return it in accordance with MPEP §609.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, material to patentability as defined in §1.56.



This statement qualifies under 37 C.F.R. §1.97(b) because (check all that apply):

- ☐ (1) It is being filed within 3 months of the application filing date and is other than a continued prosecution application under § 1.53(d)  
-- OR --
- ☐ (2) It is being filed within 3 months of entry of a national stage  
-- OR --
- ☐ (3) It is being filed before the mail date of the first Office Action on the merits  
-- OR --
- ☒ (4) It is being filed before the mailing of a first Office Action after the filing of a request for continued examination under § 1.114.

- ☐ 37 C.F.R. §1.97(c). If this statement is being filed after the latest of: (1) three months beyond the filing date of a national application; (2) three months beyond the date of entry of the national stage as set forth in §1.491 in an international application; or (3) the mailing date of a first Office action on the merits, but before the mailing date of the earlier of a final office action under §1.113 or a notice of allowance under §1.311, then:

- ☐ a certification as specified in §1.97(e) is provided below; or
- ☐ a fee of \$180.00 as set forth in §1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.

- ☐ 37 C.F.R. §1.97(d). If this statement is being filed after the mailing date of the earlier of a final office action under §1.113 or a notice of allowance under §1.311, but before payment of the issue fee, then:

- A. a certification as specified in §1.97(e) is completed below; and
- B. a petition under 37 C.F.R. §1.97(d) requesting consideration of this statement is submitted herewith; and
- C. a fee of \$130.00 as set forth in §1.17(i)(1) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.

- ☒ **Fee Authorization.** The Commissioner is hereby authorized to charge the above-referenced fees of \$0.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 08-1641 (Attorney's Docket No. 39749-0002APC).

Dated: March 2, 2005

Respectfully submitted,

By: 

Daniel M. Becker (Reg. No. 38,376)

For: Ginger R. Dreger (Reg. No. 33,055),  
Attorney of record

**HELLER EHRMAN WHITE & McAULIFFE LLP**  
275 Middlefield Road  
Menlo Park, CA 94025-3506



<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	09/214,371
				Filing Date	March 26, 1999
				First Named Inventor	David P. Lane
				Art Unit	1635
				Examiner Name	Zara, Jane J.
				Attorney Docket Number	39749-0002 US
Sheet	1	of	5		

**U.S. PATENT DOCUMENTS**

*Examiner Initials	Cite No.	DOCUMENT NUMBER Number - Kind Code (if known) <sup>2</sup>	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	US 5,411,860	05-02-1995	Vogelstein <i>et al.</i>	
	A2	US 5,519,118	05-21-1996	Vogelstein <i>et al.</i>	
	A3	US 5,532,348	07-02-1996	Huibregtse <i>et al.</i>	
	A4	US 5,550,023	08-27-1996	Kinzler <i>et al.</i>	
	A5	US 5,606,044	02-25-1997	Burrell <i>et al.</i>	
	A6	US 5,618,921	04-08-1997	Burrell <i>et al.</i>	

**FOREIGN PATENT DOCUMENTS**

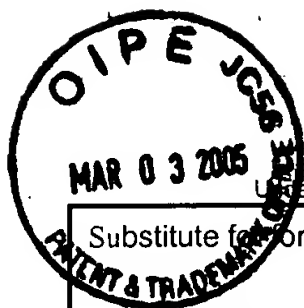
*Examiner Initials	Cite No.	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	B1	PCT WO 94/00601	01-06-1994	Levine <i>et al.</i>		
	B2	PCT WO 94/08241	04-14-1994	Zentgraf <i>et al.</i>		
	B3	PCT WO 94/10306	05-11-1994	Soussi <i>et al.</i>		
	B4	PCT WO 98/01467	01-15-1998	Lane <i>et al.</i>		
	B5	PCT WO 98/13064	04-02-1998	Lu <i>et al.</i>		

EXAMINER SIGNATURE

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Substitute for Form 1449/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

**Complete if Known**

Application Number	09/214,371
Filing Date	3/26/1999
First Named Inventor	David P. Lane
Art Unit	1635
Examiner Name	Zara, Jane J.
Attorney Docket Number	39749-0002 US

Sheet

2

of

5

**OTHER DOCUMENTS – NON-PATENT LITERATURE DOCUMENTS**

*Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	C1	Barak, Y. <i>et al.</i> , "mdm2 expression is induced by wild type p53 activity," EMBO J., 12(2): 461-468, Feb 1993	
	C2	Barak Y & Oren M., "Enhanced binding of a 95 kDa protein to p53 in cells undergoing p53-mediated growth arrest," EMBO J., 11(6): 2115-2121, Jun 1992	
	C3	Böttger A. <i>et al.</i> , "Design of a synthetic Mdm2-binding mini protein that activates the p53 response <i>in vivo</i> ," Curr. Biol., 7: 860-869, Oct 1997	
	C4	Brown D.R. <i>et al.</i> , "The tumor suppressor p53 and the oncoprotein simian virus 4D T antigen bind to overlapping domains on the MDM2 protein," Mol. Cell. Biol., 13(11): 6849-6857, Nov 1993	
	C5	Cahilly-Snyder L. <i>et al.</i> , "Molecular analysis and chromosomal mapping of amplified genes isolated from a transformed mouse 3T3 cell line," Somatic Cell Mol. Genet., 13 (3): 235-244, May 1987	
	C6	Chen C.Y. <i>et al.</i> , "Interactions between p53 and MDM2 in a mammalian cell cycle checkpoint pathway," PNAS USA, 91(7): 2684-2688, Mar 1994	
	C7	Chen J. <i>et al.</i> , "Mapping of the p53 and mdm-2 interaction domains," Mol. Cell Biol., 13: 4107-4114, Jul 1993	
	C8	Colas P. <i>et al.</i> , "Genetic selection of peptide aptamers that recognize and inhibit cyclin-dependent kinase 2," Nature, 380: 548-550, Apr 1996	
	C9	Deffie A. <i>et al.</i> , "The tumor suppressor p53 regulates its own transcription," Mol. Cell. Biol., 13: 3415-3423, Jun 1993	
	C10	Dyson N. <i>et al.</i> , "Adenovirus E1A makes two distinct contacts with the retinoblastoma protein," J. Virology, 66: 4606-4611, Jul 1992	
	C11	Dyson N. <i>et al.</i> , "Homologous sequences in adenovirus E1A and human papillomavirus E7 proteins mediate interaction with the same set of cellular proteins," J. Virology, 66: 6893-6902, Dec 1992	
	C12	Farmer G. <i>et al.</i> , "Wild-type p53 activates transcription <i>in vitro</i> ," Nature, 358: 83-86, Jul 1992	

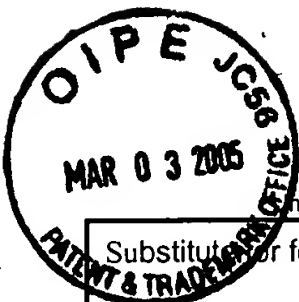
EXAMINER SIGNATURE

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:  
Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Substitute for form 1449/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

**Complete if Known**

Application Number	09/214,371
Filing Date	3/26/1999
First Named Inventor	David P. Lane
Art Unit	1635
Examiner Name	Zara, Jane J.
Attorney Docket Number	39749-0002 US

Sheet 3 of 5

**OTHER DOCUMENTS – NON-PATENT LITERATURE DOCUMENTS**

*Examiner Initials	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	C13	Finlay, C.A., "The mdm-2 Oncogene can overcome wild-type p53 suppression of transformed cell growth," Mol. Cell. Biol., 13(1): 301-306, Jan 1993	
	C14	Florenes V.A. <i>et al.</i> , "MDM2 gene amplification and transcript levels in human sarcomas: Relationship to TP53 gene status," J. Nat. Cancer Institute, 86(17): 1297-1302, Sep 1994	
	C15	Funk W. D. <i>et al.</i> , "A transcriptionally active DNA-binding site for human p53 protein complexes," Mol. Cell. Biol., 12(6): 2866-2871, Jun 1992	
	C16	Garcia-Echeverria C. <i>et al.</i> , "Structure activity studies of peptide inhibitors of the p53-HDM2 interaction," 15 <sup>th</sup> American Peptide Symposium, Jan 1997	
	C17	Haupt Y. <i>et al.</i> , "Cell type-specific inhibition of p53-mediated apoptosis by mdm2," EMBO J., 15(7): 1596-1606, Apr 1996	
	C18	Hupp T.R. <i>et al.</i> , "Small peptides activate the latent sequence-specific DNA binding function of p53," Cell, 83: 237-245, Oct 1995	
	C19	Jones S.N. <i>et al.</i> , "Rescue of embryonic lethality in Mdm-1 deficient mice by absence of p53," Nature, 378: 206-208, Nov 1995	
	C20	Juven T. <i>et al.</i> , "Wild type p53 can mediate sequence-specific transactivation of an internal promoter within the mdm2 gene," Oncogene, 8(12): 3411-3416, Dec 1993	
	C21	Kern S.E. <i>et al.</i> , "Oncogenic forms of p53 inhibit p53-regulated gene expression," Science, 256: 827-830, May 1992	
	C22	Kovar H. <i>et al.</i> , "Narrow spectrum of infrequent p53 mutations and absence of MDM2 amplification in Ewing tumours," Oncogene, 8(10): 2683-90, Oct 1993	
	C23	Kussie P.H. <i>et al.</i> , "Structure of the MDM2 oncoprotein bound to the p53 tumor suppressor transactivation domain," Science, 274: 948-953, Nov 1996	
	C24	LaVallie E.R. <i>et al.</i> , "A thioredoxin gene fusion expression system the E. coli cytoplasm," Biotechnology, 11(2): 187-193, Feb 1993	
	C25	Lane D. <i>et al.</i> , "On the regulation of the p53 tumour suppressor, and its role in the cellular response to DNA damage," Phil. Trans. R. Soc. Lond. B, 347: 83-87, 1995	

EXAMINER SIGNATURE

DATE CONSIDERED

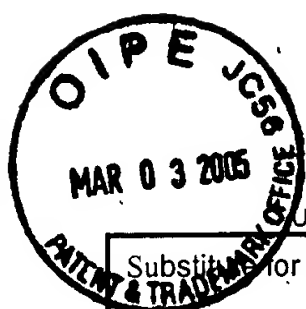
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



Substitute for form 1449/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

**Complete if Known**

Application Number	09/214,371
Filing Date	3/26/1999
First Named Inventor	David P. Lane
Art Unit	1635
Examiner Name	Zara, Jane J.
Attorney Docket Number	39749-0002 US

Sheet 4 of 5

**OTHER DOCUMENTS – NON-PATENT LITERATURE DOCUMENTS**

*Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	C26	Lees-Miller S.P. <i>et al.</i> , "Human DNA-activated protein kinase phosphorylates serines 15 and 37 in the amino-terminal transactivation domain of human p53," Mol. Cell Biol., 12(11):5041-5049, Nov 1992	
	C27	Lin J. <i>et al.</i> , "Functions of the p53 protein in growth regulation and tumor suppression," Cold Spring Harbor Symposia on Qualitative Biology, LIX: 215-223, 1994	
	C28	Lin Y & Green M., "Similarities between prokaryotic and eukaryotic cyclic AMP-responsive promoter elements," Nature, 340: 656-659, Aug 1989	
	C29	Liu X. <i>et al.</i> , "The p53 activation domain binds the TATA box-binding polypeptide in holo-TFIID, and a neighboring p53 domain inhibits transcription," Mol. Cell. Biol., 13: 3291-3300, Jun 1993	
	C30	Lu X. & Lane D., "Differential induction of transcriptionally active p53 following UV or ionizing radiation: Defects in chromosome instability syndromes?," Cell, 75: 765-778, Nov 1993	
	C31	Martin K. <i>et al.</i> , "Stimulation of E2F1/DP1 transcriptional activity by MDM2 oncoprotein," Nature, 375: 691-698, Jun 1995	
	C32	Marston N.J. <i>et al.</i> , "Interaction of p53 with MDM2 is independent of E6 and does not mediate wild type transformation suppressor function," Oncogene, 9: 2707-2716, Sep 1994	
	C33	Michalovita D. <i>et al.</i> , "Conditional inhibition of transformation and of cell proliferation by a temperature-sensitive mutant of p53," Cell, 62: 671-680, Aug 1990	
	C34	Midgley C.A. <i>et al.</i> , "Analysis of p53 expression in human tumours: an antibody raised against human p53 expressed in Escherichia coli," J. Cell Science, 101(1): 183-189, Jan 1992	
	C35	Montes de Oca Luna R. <i>et al.</i> , "Rescue of early embryonic lethality in mdm1-deficient," Nature, 378: 203-206, Nov 1995	
	C36	Oliner J.D. <i>et al.</i> , "Amplification of a gene encoding a p53-associated protein in human sarcomas," Nature, 358: 80-83, Jul 1992.	
	C37	Oliner J.D. <i>et al.</i> , "Oncoprotein MDM1 conceals the activation domain of tumour suppressor p53," Nature, 362: 857-860, Apr 1993	

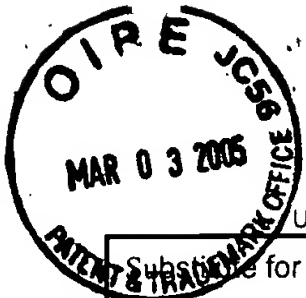
EXAMINER SIGNATURE

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	09/214,371
				Filing Date	3/26/1999
				First Named Inventor	David P. Lane
				Art Unit	1635
				Examiner Name	Zara, Jane J.
				Attorney Docket Number	39749-0002 US
Sheet	5	of	5		

**OTHER DOCUMENTS – NON-PATENT LITERATURE DOCUMENTS**

*Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	C38	Otto A. & Deppert W, "Upregulation of mdm-2 expression in meth a tumor cells tolerating wild-type p53," Oncogene, 8(9): 2591-2603, Sep 1993	
	C39	Picksley S. & Lane D., "The p53-mdm2 autoregulatory feedback loop: a paradigm for the regulation of growth control by p53," BioEssays, 15(10): 689-699, Oct 1993	
	C40	Renzing J. & Lane D., "p53-dependent growth arrest following calcium phosphate-mediated transfection of murine fibroblasts," Oncogene, 10(9): 1865-1868, May 1995	
	C41	Schlaeppli J.-M. <i>et al.</i> , "Identification of specific hdm2 binding peptides by affinity selection and mass spectrometry," 17 <sup>th</sup> International Congress of Biochemistry and Molecular Biology, San Francisco, USA, Aug 1997	
	C42	Schlichtholz B. <i>et al.</i> , "The immune response to p53 in breast cancer patients is directed against immunodominant epitopes unrelated to the mutational hot spot," Cancer Res., 52: 6380-6384, Nov 1992	
	C43	Stephen C.W. <i>et al.</i> , "Characterisation of epitopes on human p53 using phage displayed peptide libraries: Insights into antibody-peptide interactions," J. Mol. Biol., 248(1): 58-78, Apr 1995	
	C44	Unger T. <i>et al.</i> , "P53: a transdominant regulator of transcription whose function is ablated my mutations occurring in human cancer," EMBO J., 11(4): 1383-1390, Apr 1992	
	C45	Vojtesek B. & Lane D., "Regulation of p53 protein expression in human breast cancer cell lines," J. Cell Science, 105(3): 607-612, Jul 1993	
	C46	Wasylyk C. <i>et al.</i> , "P53 mediated death of cells overexpressing MDM2 by an inhibitor of MDM2 interaction with p53," Oncogene 18: 1921-1934, Mar 1999	
	C47	Wu X. <i>et al.</i> , "The p53-mdm-2 autoregulatory feedback loop," Genes & Dev., 7: 1126-1132, July 1993	

EXAMINER SIGNATURE

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S. C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.